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A new approach to ±-(trifluoromethyl)benzyl substituted oxaziridines

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ABSTRACT

The synthesis of *N*-substituted oxaziridines bearing an ±-(trifluoromethyl)benzyl substituent at C(3) was achieved by *m*-CPBA oxidation of the corresponding 3-imino-1,1,1-trifluoro-2-arylpropan-2-ols and their trimethylsilyl protected derivatives, respectively. In all cases, mixtures of diastereoisomers were formed. The prepared oxaziridine derivatives were shown to be able to oxidize thioanisole to thioanisole *S*-oxide in the presence of methanesulfonic acid.

1. Introduction

Oxaziridines are under extensive study as attractive oxidizing agents, and the so-called 'Davies oxaziridine' is the best known example [1]. In a recent paper, the first enantioselective oxidation of *N*-tosylated aryl and alkyl aldimines using *meta*-

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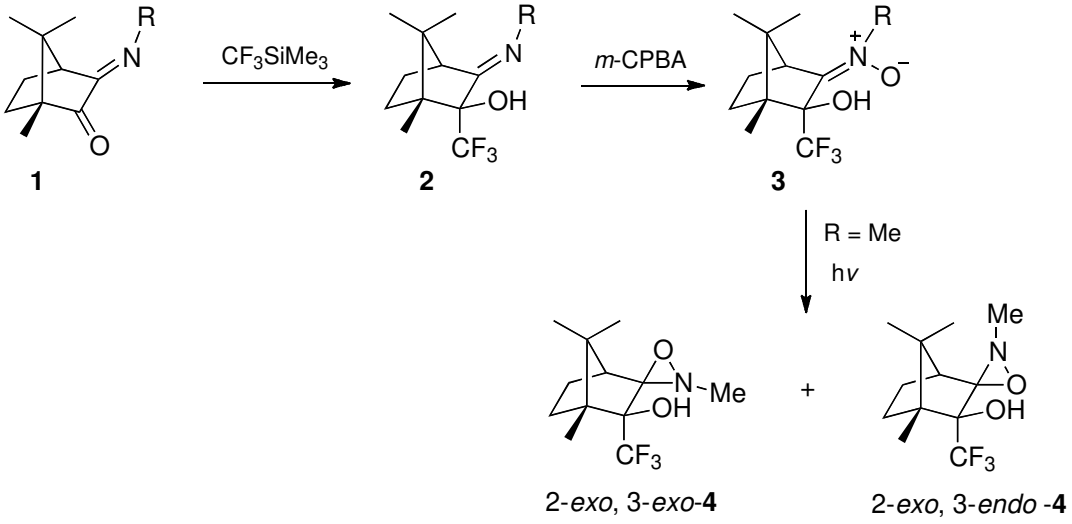
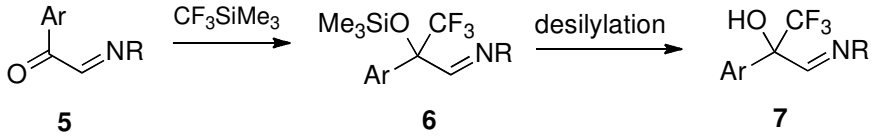
chloroperbenzoic acid (*m*-CPBA) was described [2]. On the other hand, fluorinated heterocycles are of special interest, as the introduction of a fluorinated fragment results in substantial change of physico-chemical properties, reactivity and biological activites [3]. However, fluorinated oxaziridines are less well known, and the reported examples mainly originate from perfluorinated starting materials [4]. Recently, oxaziridines derived from fluoral *N*-alkyl imines were reported [5]. Starting with enantiopure substrates, the corresponding products were obtained in a highly diastereoselective manner.

In our hands, camphorquinone monoimines **1** were reacted with (trifluoromethyl)trimethylsilane (Ruppert-Prakash reagent [6]) yielding trifluoromethylated hydroxyimines **2** chemo- and diastereoselectively [7]. Unexpectedly, the attempted oxidation of products **2** with *m*-CPBA led to nitrones **3** instead of the expected oxaziridines **4** [8] (Scheme 1). However, in one case, an oxaziridine derivative was obtained by photolysis of an isolated nitrone **3** as a mixture of the *endo* and *exo*-isomers.



Scheme 1.

In continuation of our studies on nucleophilic trifluoromethylation of α-imino ketones, reactions of arylglyoxalimines **5** were shown to yield the corresponding α-trifluoromethylated *O*-silylated hydroxyimine derivatives **6** [9] (Scheme 2).

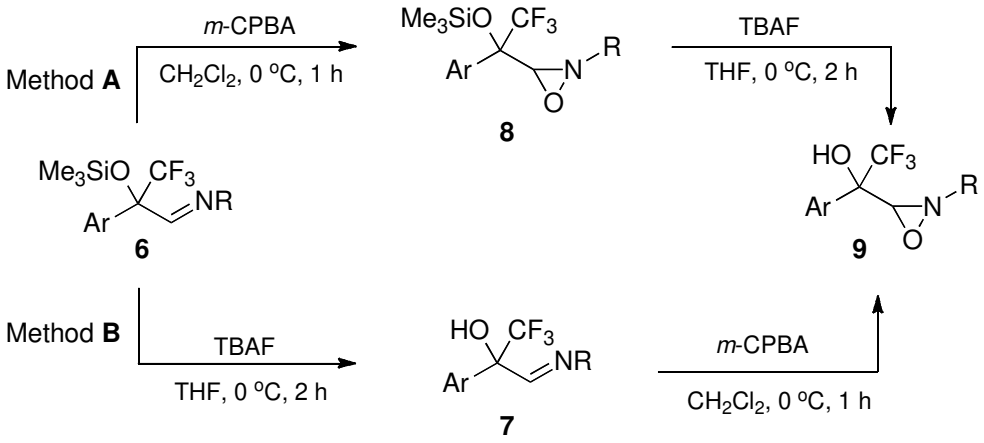


Scheme 2.

The goal of the present study was the synthesis of new α-(trifluoromethyl)benzyl-substituted oxaziridines starting with compounds **6** or the corresponding imino alcohols **7**. In addition, the oxidizing properties of this type of oxaziridines should be compared with known models of fluorine containing oxaziridines.

2. Results and discussion

Initial experiments on the oxidation of a C=N group were performed starting with the *O*-protected imino alcohols **6** [9], which after treatment with *m*-CPBA in dichloromethane at 0 °C were converted into mixtures of diastereoisomeric oxaziridines **8** in good yields (Scheme 3, Method A). The ratio of diastereoisomers (*dr*) was determined by ^{19}F-NMR spectroscopy and ranked between 9:1 and 6:4 (Table 1). Only in the case of **8e** isolation of the major isomer in pure from was successfully performed by fractional crystallization. In all other cases, neither crystallization nor chromatography allowed to separate the isomers. In order to obtain the non-protected oxaziridinyl alcohols **9**, the initially obtained products **8** were treated with tetrabutylammonium fluoride (TBAF) in THF at 0 °C. Under these conditions, in the series of the *N*-*tert*-butyl derivatives, desilylation occurred smoothly with no decomposition of the oxaziridine ring. In contrast, the *N*-isopropyl analogues led to complex mixtures of unidentified products.



Scheme 3.

Table 1. Synthesis of oxaziridines **8** and **9**.

Ar	R	**7**	Yield [%]	**8**	Yield [%]	*dr*[a)]	**9**	Yield [%]	*dr*[a)]	Method
Ph	*i*-Pr		-	**a**	70	6:4		-	-	A
		a	80		-	-	**a**	84	9:1	B
4-$MeOC_6H_4$	*i*-Pr		-	**b**	84	6:4		-	-	A
4-$NO_2C_6H_4$	*i*-Pr		-	**c**	81	8:2		-	-	A
		c	42		-	-	**c**	82	>20:1[e)]	B
4-$NO_2C_6H_4$	*t*-Bu		-	**d**	85	9:1	**d**	80	9:1	A
		d	63		-	-	**d**	87	9:1	B
Benzofuran-2-yl	*t*-Bu		-	**e**	70	8:2	**e**	79	[d)]	A
		e	[c)]		-	-	**e**	68	9:1	B

[a)] Ratio of diastereoisomers

[b)] Method A: oxidation-desilylation (via **8**); method B: desilylation-oxidation (via **7**).

[c)] Not isolated

[d)] Desilylation of major isomer of **8e**

[e)] The minor isomer was not detected using ^{19}F NMR

An alternative pathway (Method B) for the synthesis of oxaziridines **9** started with deprotection of **6** under standard conditions, and the obtained imino alcohols **7** were oxidized (Scheme 3). Using this method, both *N*-*tert*-butyl and *N*-isopropyl derivatives were obtained in good yields with comparable ratios of diastereoisomers. Again, the highest *dr* value was observed in the case of the *N*-*tert*-butyl 4-nitrobenzyl derivative **9d**.

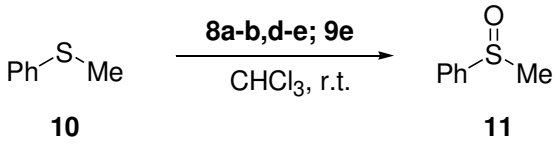
The major diastereoisomers of **9d** and **9e** were isolated as pure compounds after fractional crystallization of the crude mixtures. The spectroscopic data confirm the structure of oxaziridines **9**. For example, the ^{13}C-NMR spectrum of **9d** showed the signal of C(3) of the oxaziridine ring at 73.4 as a quartet ($^{3}J_{C,F}$ = 1.5 Hz). The CF_3 group absorbed at 124.3 ppm ($^{1}J_{C,F}$ = 285.3 Hz) and the benzylic C-atom appeared at 74.1 ppm ($^{2}J_{C,F}$ = 28.7 Hz). Furthermore, the ^{19}F-NMR spectrum showed the signal of the CF_3 group at –76.6 ppm.

Unfortunately, attempts to grow crystals suitable for X-ray crystallography with the aim of determining the absolute configuration in both cases, **9d** and **9e**, were unsuccessful.

It is worth mentioning that oxaziridines **9** are stable compounds and don't undergo decomposition during storage in the refrigerator neither as solid materials nor in solution.

The application of oxaziridines for oxidations of sulfides and N-heterocycles is well documented [1,4,10,11]. In general, oxaziridines bearing perfluorinated alkyl residues at the C-atom, are more powerful oxidizing agents in comparison with the non-fluorinated analogous [5,11].

In order to check the oxidizing properties of oxaziridines **8** and **9**, the conversion of thioanisol (**10**) into (methyl)(phenyl)sulfoxide (**11**) was examined as a model reaction. The first experiments were performed using **8d** or **9e** and **10** in a 1:1 ratio. When $CHCl_3$ was used as a solvent at room temperature, no reaction was observed even after 24 h. However, after addition of three mol-equivalents of methanesulfonic acid, the TLC control evidenced complete conversion of **10** to **11** as the sole product after 1 h at room temperature. Analogous results were observed when oxaziridines **8a**,**b**,**e** were used instead of **8d**. These experiments showed that oxaziridines **8** and **9** are only moderately active oxidizing reagents, and the oxygen transfer requires activation by a strong Brønsted acid. A similar influence of strong acids in oxidation reactions with oxaziridines has already been reported [12].



10 **11**

Scheme 4.

Table 2. Oxidation of thioanisole with oxaziridines **8** and **9e**.

Oxaziridine	Acid	Yield [%]
8d	no acid	no reaction
9e	no acid	no reaction
8a	$MeSO_3H$	70
8b	$MeSO_3H$	76
8d	$MeSO_3H$	83
8e	$MeSO_3H$	72
9e	$MeSO_3H$	80

3. Conclusions

The present study showed that the *O*-silylated imino alcohols **6**, obtained easily from glyoxal monoimines **5** via nucleophilic trifluoromethylation with Ruppert-Prakhash reagent, can be oxidized under standard conditions to give oxaziridines **8** as a mixture of diastereoisomers. After desilylation, oxaziridines **9** were obtained. Alternatively, compounds **9** can be prepared from **6** via the desilylation/oxidation sequence. These results demonstrate, that the earlier observed transformation of ±-trifluoromethyl ±-hydroxy imines **2**, derived from camphorquinone, into nitrones **3** (and not to the expected oxaziridines), upon the treatment with *m*-CPBA, results from the steric hindrance and not from the presence of the strongly electron-withdrawing CF_3 substituent.

In contrast to other fluorinated oxaziridines, derivatives **8** are less useful oxidizing reagents, which require the presence of a strong Brønsted acid to convert sulfides into

sulfoxides. Similar behavior was also observed in the case of the O-deprotected oxaziridine **9e**.

4. Experimental part

4.1. General experimental procedures

Melting points were determined on a Melt-Temp. II apparatus (Aldrich) in capillary and they are uncorrected. The ^{1}H, $^{13}C\{^{1}H\}$ and ^{19}F NMR spectra were recorded using Bruker Avance III 600 spectrometer using solvent signal as reference. Assignments of signals in ^{13}C NMR spectra were made on the basis of HMQC experiments. The IR spectra were measured using an NEXUS FT-IR spectrophotometer. The MS spectra (ESI, ESI-HRMS) were obtained using Varian 500-MS or Bruker maXis spectrometers. The EI-HRMS spectra were recorded on the Finnigan MAT 95 double focusing (BE geometry) mass spectrometer.

4.2. Materials

A commercial solution of tetrabutylammonium fluoride (TBAF, 1M in THF), *m*-chloroperbenzoic acid (*m*-CPBA), and thioanisole were purchased from Sigma-Aldrich and (trifluoromethyl)trimethylsilane from Fluorochem. ±-Iminoketones (**5a**-**5e**) were prepared according to the known protocol [9]. Dimethoxyethane (DME) was dried over sodium in the presence of benzophenone and freshly distilled prior to the use. Tetrahydrofuran (THF) was used as commercial solvent without drying.

*4.3. Reactions of ±-imino ketones **5** with (trifluoromethyl)trimethylsilane*

A solution of the corresponding ±-imino ketone **5** (1.0 mmol) in anhydrous DME (~1.5 ml), was placed in a dry, two-necked flask, equipped with septum and a tube filled with anhydrous $CaCl_2$. Next, a catalytic amount of freshly dried CsF and (trifluoromethyl)trimethylsilane (0.17 ml, 157 mg, 1.1 mmol) were added. The mixture was stirred at room temperature for ca. 1 h and subsequently quenched with water (5 ml). The solution was extracted three times with CH_2Cl_2. The organic layers were combined and dried over anhydrous Na_2SO_4. After filtration, the solvents were

evaporated and the crude, oily products **6** were used for further reactions without purification.

*4.4. Syntheses of (trifluoromethyl)oxaziridines **8** and **9***

Method A - general procedures. *Oxidation of* **6**: *m*-CPBA (70%, 250 mg, 1.1 mmol) was added in small portions to the magnetically stirred solution of the corresponding silyl ether **6** in CH_2Cl_2 (2 ml), cooled in an ice-bath. Next, the solution was stirred for ca. 2 h, and a saturated solution of K_2CO_3 was added. The mixture was extracted three times with CH_2Cl_2. The organic layers were combined and dried over anhydrous Na_2SO_4. After filtration, the solvent was evaporated and the crude oily products **8** were purified by column chromatography (SiO_2, hexane/CH_2Cl_2 7:3).

Desilylation of **8**: The flask containing a solution of compound **8** in THF (2 ml) was placed in an ice bath. Next, TBAF dissolved in THF (1 M, 1.5 ml, 1.5 mmol) was added dropwise and the mixture was stirred for ca. 3 h. Then, a portion of water was added and the mixture was extracted three times with CH_2Cl_2. The organic layers were combined and dried over anhydrous Na_2SO_4. After filtration, the solvents were evaporated, and the crude oily products **9** were purified by column chromatography (SiO_2, hexane/CH_2Cl_2 7:3).

After additional crystallization from an appropriate solvent, products **9d** and **9e** were obtained as pure diastereoisomers .

Method B - general procedures. Desilylation of **6**: To a flask placed in ice-bath and containing the corresponding silyl ether **6** in THF (2 ml), a solution of TBAF in THF (1 M, 1.5 ml, 1.5 mmol) was added and the mixture was magnetically stirred for ca. 3 h. Then, a portion of water was added and the mixture was extracted three times with CH_2Cl_2. The organic layers were combined and dried over anhydrous Na_2SO_4. After filtration, the solvents were evaporated, and the products **7** were purified by column chromatography (SiO_2, hexane/CH_2Cl_2 7:3).

Oxidation of **7**: A flask containing compound **7** dissolved in CH_2Cl_2 (2 ml) was placed in an ice bath, and *m*-CPBA (70%, 250 mg, 1.1 mmol) was added. The mixture was stirred for ca. 2 h. Next, a saturated solution of K_2CO_3 was added, and the resulting mixture was extracted three times with CH_2Cl_2. The organic layers were combined and dried over anhydrous Na_2SO_4. After filtration, the solvent was evaporated to dryness,

and the crude products **9** were obtained as viscous oils and purified by column chromatography (SiO_2, hexane/CH_2Cl_2 7:3).

3-Imino-1,1,1-trifluoro-2-arylpropan-2-ols **7**.

3-(Isopropyl)imino-1,1,1-trifluoro-2-phenylpropan-2-ol (**7a**). Yield: 196 mg (80%). Colorless, viscous oil. ^{1}H NMR (600 MHz): ´ 1.16, 1.24 (2d, $^3J_{H,H}$ = 6.6 Hz, 6H, CH(C**H**$_3$)$_2$), 3.70–3.75 (m, 1H, C**H**(CH$_3$)$_2$), 5.75 (s, 1H, OH), 7.38–7.44 (m, 3 arom. CH), 7.67–7.68 (m, 2 arom. CH), 8.10 (s, 1H, HC=N) ppm. ^{13}C NMR (150 MHz): ´ 23.4, 23.6 (CH(**C**H$_3$)$_2$), 58.6 (**C**H(CH$_3$)$_2$), 75.7 (q, $^2J_{C,F}$ = 28.5 Hz, C_q), 124.2 (q, $^1J_{C,F}$ = 285.0 Hz, CF_3), 126.4, 128.6, 128.9 (5 arom. CH), 135.3 (1 arom. C), 155.2 (C=N) ppm. ^{19}F NMR (565 MHz): ´ −77.10 (s, 3F, CF_3) ppm. IR (film): *v* 3327*br.m* (OH), 3065*w*, 2974*m*, 2933*m*, 2874*m*, 1668*m* (C=N), 1452*m*, 1386*m*, 1265*s*, 1194*s*, 1166*s*, 1017*m*, 978*m* cm^{-1}. ESI-MS: *m/z* 204 (12), 246 (100 [M+1]$^+$), 247 (12). EI-HRMS: Calcd. for $C_{12}H_{14}F_3NO^+$ (M$^+$): *m/z* 245.10223; found: *m/z* 245.10275.

3-(Isopropyl)imino-1,1,1-trifluoro-2-(4-nitrophenyl)propan-2-ol (**7c**). Yield: 122 mg (42%). Colorless crystals, m.p. 70–72 °C (Et_2O/hexane). ^{1}H NMR (600 MHz): ´ 1.17, 1.25 (2d, $^3J_{H,H}$ = 6.6 Hz, 6H, CH(C**H**$_3$)$_2$), 3.74–3.78 (m, 1H, C**H**(CH$_3$)$_2$), 5.86 (s, 1H, OH), 7.87–7.88 (m, 2 arom. CH), 8.08 (s, 1H, HC=N), 8.27–8.29 (m, 2 arom. CH) ppm. ^{13}C NMR (150 MHz): ´ 23.6, 23.7 (CH(**C**H$_3$)$_2$), 58.9 (**C**H(CH$_3$)$_2$), 76.1 (q, $^2J_{C,F}$ = 30.2 Hz, C_q), 123.9, 127.8 (4 arom. CH), 124.0 (q, $^1J_{C,F}$ = 286.8 Hz, CF_3), 142.4, 148.6 (2 arom. C), 154.0 (**C**=N) ppm. ^{19}F NMR (565MHz): ´ −76.87 (s, 3F, CF_3) ppm. IR (KBr): *v* 3343*br.m* (OH), 3166*w*, 2981*m*, 2879*w*, 1667*m*, 1516*s* (C=N), 1534*s*, 1266*s*, 1197*s*, 1161*s*, 1017*m* cm^{-1}. ESI-MS: *m/z* 291 (100, [M+1]$^+$), 292 (10). EI-HRMS: Calcd. for $C_{12}H_{13}F_3N_2O_3^+$ (M$^+$): *m/z* 290.08796; found: *m/z* 290.08783.

3-(tert-Butyl)imino-1,1,1-trifluoro-2-(4-nitrophenyl)propan-2-ol (**7d**). Yield: 192 mg (63%). Colorless crystals, m.p. 97–99 °C (CH_2Cl_2/hexane). ^{1}H NMR (600 MHz): ´ 1.25 (s, 9H, C(CH$_3$)$_3$), 7.87–7.89, 8.27–8.28 (2m, 4 arom. CH), 7.98 (s, 1H, HC=N) ppm. ^{13}C NMR (150 MHz): ´ 29.2 (C(**C**H$_3$)$_3$), 58.0 (**C**(CH$_3$)$_3$), 74.1 (q, $^2J_{C,F}$ = 30.1 Hz, C_q), 123.8 (q, $^1J_{C,F}$ = 285.3 Hz, CF_3), 123.7, 127.6 (4 arom. CH), 142.4, 148.3 (2 arom. C), 150.8 (C=N) ppm. ^{19}F NMR (565MHz, $CDCl_3$): ´ −76.79 (s, 3F, CF_3) ppm. IR (KBr): *v* 3312*br.m* (OH), 2972*m*, 2944*w*, 2877*w*, 1668*w*, 1600*w*, 1518*vs* (C=N), 1418*w*, 1352*s*, 1264*s*, 1191*vs*, 1152*vs*, 1111*m*, 1012*m*, 970*m* cm^{-1}. ESI-HRMS: Calcd. for

$C_{13}H_{15}F_3N_2O_3Na^+$ ([M+23]$^+$): *m/z* 327.09270; found: *m/z* 327.09279. Calcd. for $C_{13}H_{16}F_3N_2O_3^+$ ([M+1]$^+$): *m/z* 305.11075; found: *m/z* 305.11078.

(Trifluoromethyl)(trimethylsilyloxy)oxaziridines ***8***.

N-Isopropyl-3-[2,2,2-trifluoro-1-phenyl-1-(trimethylsilyloxy)ethyl]oxaziridine (**8a**). Yield: 233 mg (70%). Colorless, viscous oil. Compound isolated as a mixture of diastereomers (6:4). ^{1}H NMR (600 MHz): ´ major diastereomer: 0.13 (s, 9H, Si(CH$_3$)$_3$), 1.14, 1.28 (2d, $^3J_{H,H}$ = 6.6 Hz, 6H, CH(C**H**$_3$)$_2$), 4.39 (s, 1H, OCHN); minor diastereomer: 0.19 (s, 9H, Si(CH$_3$)$_3$), 0.96 (d, $^3J_{C,H}$ = 6.6 Hz, 3H, CH(C**H**$_3$)$_2$), 1.21 (d, $^3J_{H,H}$ = 6.2 Hz, 3H, CH(C**H**$_3$)$_2$), 4.38 (s, 1H, OCHN); both diastereomers: 2.23–2.32 (m, 1H, C**H**(CH$_3$)$_2$), 7.37–7.42 (m, 3 arom. CH), 7.59–7.61 (m, 2 arom. CH) ppm. ^{13}C NMR (150 MHz): ´ major diastereomer: 2.31 (Si(CH$_3$)$_3$), 62.7 (**C**H(CH$_3$)$_2$), 78.2 (q, $^2J_{C,F}$ = 34.7Hz, C$_q$), 81.6 (OCHN) 124.6 (q, $^1J_{C,F}$ = 288.3 Hz, CF$_3$), 136.1 (1 arom. C); minor diastereomer: 2.37 (Si(CH$_3$)$_3$), 62.5 (**C**H(CH$_3$)$_2$), 78.4 (q, $^2J_{C,F}$ = 28.7 Hz, C$_q$), 81.3 (OCHN) 124.7 (q, $^1J_{C,F}$ = 286.8 Hz, CF$_3$), 135.1 (1 arom. C); both diastereomers: 18.70, 18.73, 21.43, 21.48 (CH(**C**H$_3$)$_2$), 127.4, 128.2, 128.5, 129.1, 129.3 (5 arom. CH) ppm. ^{19}F NMR (565 MHz): ´ major diastereomer: −75.7 (s, 3F, C**F**$_3$); minor diastereomer: −76.2 (s, 3F, CF$_3$) ppm. IR (film): *ν* 3065*w*, 2977*m*, 2899*w*, 1498*w*, 1451*m*, 1253*m*, 1170*m*, 1027*m*, 847*m* cm^{-1}. ESI-MS: *m/z* 330 (25), 331 (65), 332 (100, [M–1]$^+$), 352 (65), 352 (67), 353 (90).

N-Isopropyl-3-[2,2,2-trifluoro-1-(4-methoxyphenyl)-1-(trimethylsilyloxy)ethyl]-oxaziridine (**8b**). Yield: 305 mg (84%). Colorless, viscous oil. Compound isolated as a mixture of diastereomers (6:4). ^{1}H NMR (600 MHz): ´ major diastereomer: 0.11 (s, 9H, Si(CH$_3$)$_3$), 1,14, 1.27 (2d, $^3J_{H,H}$ = 6.6 Hz, 6H, CH(C**H**$_3$)$_2$), 3.83 (s, 3H, CH$_3$O), 4.35 (s, 1H, OCHN); minor diastereomer: 0.19 (s, 9H, Si(CH$_3$)$_3$), 1.00, 1.22 (2d, $^3J_{H,H}$= 6.6 Hz, 6H, CH(C**H**$_3$)$_2$), 3.82 (s, 3H, CH$_3$O), 4.34 (s, 1H, OCHN); both diastereomers: 2.24–2.31 (m, 1H, C**H**(CH$_3$)$_2$), 6.88–6.93, 7.47–7.52 (2m, 4 arom. CH) ppm. ^{13}C NMR (150 MHz): ´ major diastereomer: 2.28 (Si(CH$_3$)$_3$), 55.42 (OCH$_3$), 62.64 (**C**H(CH$_3$)$_2$), 77.9 (q, $^2J_{C,F}$ = 27.2 Hz, C$_q$), 81.6 (OCHN), 124.6 (q, $^1J_{C,F}$ = 288.3 Hz, CF$_3$), 160.3 (1 arom. C); minor diastereomer: 2.34 (Si(CH$_3$)$_3$), 55.37 (OCH$_3$), 62.55 (**C**H(CH$_3$)$_2$), 78.2 (q, $^2J_{C,F}$ = 27.2 Hz, C$_q$), 81.3 (OCHN), 124.7 (q, $^1J_{C,F}$ = 286.8 Hz, CF$_3$), 160.2 (1 arom. C); both diastereomers: 18.7, 18.8, 21.4, 21.5 (CH(**C**H$_3$)$_2$), 113.5, 113.8, 128.74, 128.77, 128.8 (5 arom. CH), 126.9, 128.0 (1 arom. C) ppm. ^{19}F NMR (565 MHz): ´ major

diastereomer: −75.9 (s, 3F, CF_3); minor diastereomer: −76.5 (s, 3F, CF_3) ppm. IR (film): *v* 3047*w*, 2976*m*, 2901*m*, 2841*w*, 1771*w*, 1613*m*, 1515*m*, 1466*m*, 1254*s*, 1166*s*, 1032*m* cm^{-1}. ESI-MS: *m/z* 364 (100, $[M+1]^+$), 386 (70, $[M+23]^+$). EI-HRMS Calcd. for $C_{16}H_{24}F_3NO_3Si^+$ (M^+): *m/z* 363.14658; found: *m/z* 363.14776.

N-Isopropyl-3-[2,2,2-trifluoro-1-(4-nitrophenyl)-1-(trimethylsilyloxy)ethyl]-oxaziridine (**8c**). Yield: 306 mg (81%). Yellow, viscous oil. Compound isolated as a mixture of diastereomers (8:2). ^{1}H NMR (600 MHz): ´ major diastereomer: 0.21 (s, 9H, $Si(CH_3)_3$), 1.14 (d, $^3J_{H,H}$ = 6.6 Hz, 3H, $CH(C\mathbf{H}_3)_2$), 1.25 (d, $^3J_{H,H}$ = 6.0 Hz, 3H, $CH(C\mathbf{H}_3)_2$), 4.34 (s, 1H, OCHN), 8.23–8.26 (m, 2 arom. CH); minor diastereomer: 0.26 (s, 9H, $Si(CH_3)_3$), 1.06 (d, $^3J_{H,H}$ = 6.6Hz, 3H, $CH(C\mathbf{H}_3)_2$), 1.21 (d, $^3J_{H,H}$ = 6.0 Hz, 3H, $CH(C\mathbf{H}_3)_2$), 4.34 (s, 1H, OCHN), 8.20–8.22 (m, 2 arom. C**H**); both diastereomers: 2.26–2.34 (m, 1H, $C\mathbf{H}(CH_3)_2$), 7.77–7.81 (m, 2 arom. CH) ppm. ^{13}C NMR (150 MHz): ´ major diastereomer: 2.3 ($Si(CH_3)_3$), 62.6 ($\mathbf{C}H(CH_3)_2$), 78.5 (q, $^2J_{C,F}$ = 27.2 Hz, C_q), 81.0 (OCHN), 124.1 (q, $^1J_{C,F}$ = 288.3 Hz, CF_3), 148.6 (1 arom. C); minor diastereomer: 2.2 ($Si(CH_3)_3$), 62.7 ($\mathbf{C}H(CH_3)_2$), 80.5 (OCHN), 78.9 (q, $^2J_{C,F}$ = 28.5 Hz, C_q), 148.5 (1 arom. C); both diastereomers: 18.6, 18.8, 21.3 ($CH(\mathbf{C}H_3)_2$), 113.5, 113.8, 128.74, 128.77, 128.8 (5 arom. CH), 126.9, 128.0 (1 arom. C) ppm. The CF_3 signal for the minor product could not be found. ^{19}F NMR (565 MHz): ´ major diastereomer: −74.9 (s, 3F, CF_3); minor diastereomer: −75.7 (s, 3F, CF_3) ppm. IR (film): *v* 3085*w*, 2977*m*, 2900*m*, 2459*w*, 1941*w*, 1771*w*, 1609*s*, 1351*s*, 1254*s*, 1174*s*, 1119*w* cm^{-1}. ESI-MS: *m/z* 306 (18), 352 (12), 379 (100, $[M+1]^+$), 382 (18). EI-HRMS: Calcd. for $C_{15}H_{22}F_3N_2O_4Si^+$ ($[M+1]^+$): *m/z* 379.13013; found: *m/z* 379.13010.

N-(tert-Butyl)-3-[2,2,2-trifluoro-1-(4-nitrophenyl)-1-(trimethylsilyloxy)ethyl]-oxaziridine (**8d**). Yield: 333mg (85%); isolated as a mixture of diastereomers (9:1). Colorless oil. ^{1}H NMR (600 MHz): ´ major diastereomer: 0.24 (s, 9H, $Si(CH_3)_3$), 1.14 (s, 9H, $C(CH_3)_3$), 4.52 (s, 1H, OCHN), 7.80–7.82, 8.26–8.29 (2m, 4 arom. C**H**); minor diasteromer: 0.29 (s, 9H, $Si(CH_3)_3$), 1.22 (s, 9H, $C(CH_3)_3$), 4.55 (s, 1H, OCHN), 7.83–7.85, 8.31–8.33 (2m, 4 arom. CH) ppm. ^{13}C NMR (150 MHz): ´ major diastereomer: 2.4 ($Si(CH_3)_3$), 25.3 ($C(\mathbf{C}H_3)_3$), 59.0 ($\mathbf{C}(CH_3)_3$), 74.8 (OCHN), 78.7 (q, $^2J_{C,F}$ = 28.7 Hz, C_q), 124.2 (q, $^1J_{C,F}$ = 288.3 Hz, CF_3), 123.3, 128.6 (4 arom. CH), 142.7, 148.5 (2 arom. C). Due to low intensities, absorption signals of the minor diastereomer could not be determined. ^{19}F NMR (565 MHz): ´ major diastereomer: –74.9 (s, CF_3); minor diastereomer: –75.9 (s, CF_3) ppm. IR (KBr): *v* 2980*m*, 2904*w*, 1525*s*, 1351*vs*, 1303*s*,

1292*s*, 1252*s*, 1178*vs*, 1045*m*, 1015*m*, 850*m* cm^{-1}. ESI-HRMS: Calcd. for $C_{16}H_{23}F_3NO_4SiNa^+$ ($[M+23]^+$): *m/z* 415.12714; found: *m/z* 415.12729.

N-(tert-Butyl)-3-[1-(benzofuran-2-yl)-2,2,2-trifluoro-1-(trimethylsilyloxy)ethyl]-oxaziridine (**8e**). Yield: 0.271g (70%). Colorless crystals, m.p. 65–67 °C (hexane). The product was isolated as a single diastereomer after fractional crystallization. ^{1}H NMR (600 MHz): ´ 0.11 (s, 9H, $Si(CH_3)_3$), 1.15 (s, 9H, $C(C\mathbf{H}_3)_3$), 4.65 (s, 1H, OCHN), 6.95 (s, 1H, 1 arom. CH), 7.26–7.28, 7.33–7.36, 7.52–7.54, 7.60–7.61 (4m, 4 arom. CH) ppm. ^{13}C NMR (150 MHz): ´ 1.7 ($Si(CH_3)_3$), 25.3 ($C(\mathbf{C}H_3)_3$), 58.8 ($\mathbf{C}(CH_3)_3$), 74.4 (OCHN), 75.9 (q, $^2J_{C,F}$ = 28.7 Hz, C_q), 107.8, 111.8, 121.9, 123.5, 125.4 (5 arom. CH), 123.8 (q, $^1J_{C,F}$ = 288.3 Hz, CF_3), 127.7, 150.8, 154.9 (3 arom. C) ppm. ^{19}F NMR (565 MHz): ´ –76.5 (s, CF_3) ppm. IR (KBr): *v* 2982*m*, 2962*m*, 1454*w*, 1365*w*, 1294*s*, 1251*s*, 1204*vs*, 1155*vs*, 1142*vs*, 1045*m*, 1024*m*, 990*m* cm^{-1}. ESI-HRMS: Calcd. for $C_{18}H_{24}F_3NO_3Na^+$ ($[M+23]^+$): *m/z* 410.13698; found: *m/z* 410.13714.

(Trifluoromethyl)(hydroxy)oxaziridines ***9***.

N-Isopropyl-3-(2,2,2-trifluoro-1-phenyl-1-hydroxyethyl)oxaziridine (**9a**). Yield: 0.219g (84%); isolated as a mixture of diastereomers (9:1). Colorless, viscous oil. ^{1}H NMR (600 MHz, $CDCl_3$): ´ major diastereomer: 1.14, (d, $^3J_{H,H}$ = 6.6 Hz, 3H, $CH(C\mathbf{H}_3)_2$), 2.38–2.45 (m, 1H, $C\mathbf{H}(CH_3)_2$), 3.55 (s, 1H, OH), 4.48 (s, 1H, OCHN); minor diastereomer: 1.11 (d, $^3J_{H,H}$ = 6.6 Hz, 3H, $CH(C\mathbf{H}_3)_2$), 2.17–2.23 (m, 1H, $C\mathbf{H}(CH_3)_2$), 3.18 (s, 1H, OH), 4.43 (s, 1H, OCHN); both diastereomers: 1.19–1.22 (m, 6H, $CH(C\mathbf{H}_3)_2$), 7.30–7.37, 7.55–7.59 (2m, 5 arom., CH) ppm. ^{13}C NMR (150 MHz): ´ major diastereomer: 18.3, 21.2 ($CH(\mathbf{C}H_3)_2$), 61.2 ($\mathbf{C}H(CH_3)_2$), 73.7 (q, $^2J_{C,F}$ = 28.7Hz, C_q), 79.2 (OCHN), 124.6 (q, $^1J_{C,F}$ = 268.7 Hz, CF_3), 133.4 (1 arom. C); minor diastereomer: 18.1, 21.0 ($CH(\mathbf{C}H_3)_2$), 61.7 ($\mathbf{C}H(CH_3)_2$), 79.8 (OCHN), 126.9 (q, $^1J_{C,F}$ = 286.8 Hz, CF_3), 133.7 (1 arom. C); both diastereomers: 126.4, 128.6, 129.2 (5 arom. CH) ppm. Due to low intensity, the signal for C(2') could not be found. ^{19}F NMR (565 MHz, $CDCl_3$): ´ major diastereomer: –76.94 (3F, CF_3); minor diastereomer: –76.93 (3F, CF_3) ppm. IR (film): *v* 3473 *br.m* (OH), 3066*w*, 2979*m*, 2933*m*, 1454*m*, 1373*m*, 1292*m*, 1201*s*, 1164*s*, 1007*m* cm^{-1}. ESI-MS: *m/z* 262 (50, $[M+1]^+$), 284 (100, $[M+23]^+$).

N-Isopropyl-3-[2,2,2-trifluoro-1-(4-nitrophenyl)-1-hydroxyethyl]oxaziridine (**9c**). Yield: 0.251g (82%); obtained as a single diastereomer. Yellowish, viscous oil. ^{1}H

NMR (600 MHz, $CDCl_3$): ´ 1.16 (d, $^3J_{H,H}$ = 6.6 Hz, 3H, CH(C**H**$_3$)$_2$), 1.22 (d, $^3J_{H,H}$ = 6.0 Hz, 3H, CH(C**H**$_3$)$_2$), 2.43–2.49 (m, 1H, C**H**(CH$_3$)$_2$), 3.74 (s, 1H, OH), 4.50 (s, 1H, OCHN), 7.76–7.78, 8.20–8.22 (2m, 4 arom. CH) ppm. ^{13}C NMR (150 MHz): ´ 18.3, 21.1 (CH(**C**H$_3$)$_2$), 61.2 (**C**H(CH$_3$)$_2$), 73.9 (q, $^2J_{C,F}$ = 28.7 Hz, C_q), 78.6 (OCHN), 124.1 (q, $^1J_{C,F}$ = 288.3 Hz, CF_3), 123.6, 127.8 (4 arom. CH), 140.2, 148.6 (2 arom. C) ppm. ^{19}F NMR (565 MHz, $CDCl_3$): ´ –76.7 (s, 3F, CF_3) ppm. IR (KBr): *v* 3385 *br.m*, (OH), 3118*w*, 1610*m*, 1526*s*, 1353*s*, 1173*s*, 1058*m* cm^{-1}.

N-(tert-Butyl)-3-[2,2,2-trifluoro-1-(4-nitrophenyl)-1-hydroxyethyl]oxaziridine (**9d**). Yields: 0.256g (80%, method A), 0.262g (82%, method B); isolated as a single diastereomer after additional crystallization. Colorless crystals, m.p. 116–119 °C (hexane/Et_2O). ^{1}H NMR (600 MHz): ´ 1.18 (s, 9H, C(C**H**$_3$)$_3$), 4.08 (s, 1H, OH), 4.69 (s, 1H, OCHN), 7.84–7.86, 8.28–8.29 (2m, 4 arom. CH) ppm. ^{13}C NMR (150 MHz): ´ 25.4 (C(**C**H$_3$)$_3$), 59.0 (**C**(CH$_3$)$_3$), 73.4 (q, $^3J_{C,F}$ = 1.5 Hz, OCHN), 74.1 (q, $^2J_{C,F}$ = 28.7 Hz, C_q), 124.3 (q, $^1J_{C,F}$ = 285.3 Hz, CF_3), 123.9, 128.0 (4 arom. CH), 140.7, 148.8 (2 arom. C) ppm. ^{19}F NMR (565 MHz): ´ –76.6 (s, CF_3) ppm. **IR** (KBr): *v* 3437*br.m* (OH), 2982*w*, 1611*m*, 1528*vs*, 1352*s*, 1274*m*, 1200*s*, 1169*vs*, 1166*s*, 854*m* cm^{-1}. ESI-HRMS: Calcd. for $C_{13}H_{15}F_3N_2O_4Na^+$ ([M+23]$^+$): *m/z* 343.08761; found: *m/z* 343.08728.

N-(tert-Butyl)-3-[1-(benzofuran-2-yl)-2,2,2-trifluoro-1-hydroxyethyl]oxaziridine (**9e**). Yields: 0.214g (68%, method B), 0.249g (79%, method A); isolated as a single diastereomer after fractional crystallization. Colorless crystals, m.p. 70–72 °C (hexane). ^{1}H NMR (600 MHz): ´ 1.20 (s, 9H, C(C**H**$_3$)$_3$), 3.87 (s, 1H, OH), 4.85 (s, 1H, OCHN), 7.03 (s, 1H, 1 arom. CH), 7.26–7.28, 7.33–7.36, 7.54–7.55, 7.61–7.62 (4m, 4 arom. CH) ppm. ^{13}C NMR (150 MHz): ´ 25.4 (C(**C**H$_3$)$_3$), 59.0 (**C**(CH$_3$)$_3$), 72.3 (q, $^3J_{C,F}$ = 1.5 Hz, OCHN), 72.8 (q, $^2J_{C,F}$ = 29.7 Hz, C_q), 107.7, 111.8, 121.9, 123.3, 125.3 (5 arom. CH), 123.8 (q, $^1J_{C,F}$ = 287.2 Hz, CF_3), 127.5, 149.7, 155.7 (3 arom. C) ppm. ^{19}F NMR (565 MHz): ´ –77.0 (s, CF_3) ppm. IR (KBr): *v* 3481*br.m* (OH), 2983*m*, 2971*w*, 1455*w*, 1370*m*, 1281*m*, 1194*s*, 1160*vs*, 1136*m*, 999*m* cm^{-1}. ESI-HRMS: Calcd. for $C_{15}H_{16}F_3NO_3Na^+$ ([M+23]$^+$): *m/z* 338.09745; found: *m/z* 338.09757.

4.5. Oxidation of thioanisole with (trifluoromethyl)oxaziridines - general procedure.

The corresponding (trifluoromethyl)oxaziridine **8** or **9** (1.05 mmol) was dissolved in $CHCl_3$ and, subsequently, thioanisole (1.0 mmol) and methanesulfonic acid (3.0 mmol) were added to this solution at room temperature. The progress of the reaction was monitored by TLC, and when the reaction was finished (1-2 h), an aqueous solution of K_2CO_3 was added. The resulting mixture was extracted with CH_2Cl_2, the separated organic layers were combined, dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The obtained thioanisole *S*-oxide was purified by column chromatography (SiO_2, 9:1 hexane/ethyl acetate). Yield: 98–116 mg (70–83%), yellowish oil. ^{1}H NMR (600 MHz): ´ 2.72 (s, 3H, CH_3), 7.50-7.55 (m, 3 arom. H), 7.62-7.67 (m, 2 arom. H) ppm (lit. [13]).

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